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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,617	01/14/2005	Tommy Urban Skantze	1103326-0785	5110

7470 7590 10/27/2009

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PATENT DEPARTMENT
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EXAMINER	
TRAN, SUSAN T	
ART UNIT	PAPER NUMBER
1615	
MAIL DATE	DELIVERY MODE
10/27/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,617	SKANTZE ET AL.	
	Examiner	Art Unit	
	S. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-10 and 12-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-10 and 12-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/03/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/12/09 has been entered.

Claim Rejections - 35 USC § 103

Claims 1, 3-10 and 12-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kipp et al. US 6,607,784, in view of Luddecke et al. US 5,895,659.

Kipp teaches a process for preparing submicron size particles of an organic compound. The process comprising: 1) dissolving the organic compound in the water miscible first solvent to form a solution; 2) mixing the solution with an aqueous second solvent to precipitate the organic compound to form a pre-suspension; and 3) adding energy to the pre-suspension to form particles having an average effective particle size of 400 nm (abstract; column 4, lines 57-65; column 6, lines 32-41; and column 8). Organic compound includes pharmaceutically active compound (column 5, lines 60-67). Energy adding step includes sonicating the dispersion of amorphous particles for 15-30 minutes at temperature ranges from about -30°C to 30°C (column 7, lines 49-67; and examples). The aqueous second solvent further comprises one or more surfactants

such as polyvinyl pyrrolidone and sodium dodecyl sulfate (column 6, lines 42 through column 7, lines 1-8; column 8, lines 51-67; and examples).

Kipp does not explicitly teach the claimed mean particle size of from 10-200 nm. However, it would have been obvious to one of ordinary skill in the art to, by routine experimentation optimize the process of Kipp to prepare nanoparticle having particle size from 10-200 nm, because Kipp teaches the desirability for preparing particles having average effective size less than 400 nm (column 4, lines 49-56).

Kipp further does not expressly teach the rate of mixing such as rapid mixing in less than 30 seconds (10, 11, 13 and 20). However, it would have been obvious to one of ordinary skill in the art to, by routine experimentation modify the process of Kipp to obtain the claimed invention. This is because Kipp teaches that the process conditions such as rate of mixing of solution, rate of precipitation and the like can be selected/optimize (column 5, lines 49-55).

However, to be more specific, Luddecke is cited for the teaching that rapid mixing technique is known in the art (see column 1, lines 41-48; column 5, lines 41-50; and examples). Luddecke also teaches the use of a rapid mixing technique to obtain particle having mean particle size of 0.03 μm (column 7, lines 16-20). Thus, it would have been obvious to one of ordinary skill in the art to modify the process for preparing submicron size particle of Kipp using the rapid mixing rate in view of Luddecke to obtain particle having submicron size. This is because Luddecke teaches the use of a rapid mixing technique to form a fine suspension that is stable on storage (column 7, lines 1-

40), and because Kipp teaches the desirability for preparing a suspension with fine particle size of less than 400 nm.

Claims 1, 3-10 and 12-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lindrud et al. WO 00/44468 A1, in view of Luddecke et al. US 5,895,659.

Lindrud teaches a process for preparing submicron size crystalline comprising: combining a solution of a pharmaceutical compound to be crystallized and an aqueous phase to form a precipitation (page 4, 2nd paragraph). Lindrud further teaches the use of surfactant (page 4, 3rd paragraph). Sonicating the precipitate to obtain submicron size crystalline (pages 4-5). Example 1 discloses upon completion of crystallization, the product is filtered, washed and dried to obtain submicron particles (the claimed isolating step). Example 1 further discloses the temperature is maintained at 2°C throughout the crystallization.

Lindrud does not explicitly teach that the phases are mixed rapidly, however, Lindrud teaches that the phases are mixed at a maximum power level (see examples). Hence, the burden is shifted to applicant to show that the process of Lindrud does not provide rapid mixing. This is because Lindrud teaches a process for crystallizing submicron size particles that provides superior crystal structure when compared with particles formed by standard slow crystallization (page 2, lines 13-17). However, to be more specific, Luddecke is cited for the teaching that rapid mixing technique is known in the art (see column 1, lines 41-48; column 5, lines 41-50; and examples). Luddecke

also teaches the use of a rapid mixing technique to obtain particle having mean particle size of 0.03 μm (column 7, lines 16-20).

Thus, it would have been obvious to one of ordinary skill in the art to modify the process for preparing submicron size particle of Lindrud using the rapid mixing rate in view of Luddecke to obtain particle having submicron size. This is because Luddecke teaches the use of a rapid mixing technique to form a fine suspension that is stable on storage (column 7, lines 1-40), and because Luddecke teaches that rapid mixing technique is well known in the art.

Response to Arguments

Applicant's arguments filed 08/05/09 have been fully considered but they are not persuasive.

Applicant argues that Kipp does not teach the claimed particle size.

However, as discussed in the above 103(a) rejection, Kipp teaches the desirability for preparing a system with particle size below 400 nm, which falls within the claimed particle size range of 10-200 nm. Further, Kipp is cited in view of Luddecke for the teachings of using a rapid mixing technique to obtain particle having mean diameter of 0.03 μm (column 7, lines 16-20). In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that there is no motivation to combine Kipp with Luddecke because:

the express purpose of Luddecke is to provide finely dispersed carotenoid and retinoid suspensions in which it is possible to dispense with a protective colloid (col. 2, 11-14) As background at column 1, lines 41-56, Luddecke discusses EP-B-0 065 193 which describes: a process for preparing finely dispersed carotenoids and retinoid products in powder form US 4,522,743 to Horn et al. (the "'743 patent") belongs to the same patent family as EP-B-0 065 193. Therefore, to fulfill the express purpose of Luddecke, i.e., to dispense with a protective colloid, Luddecke cannot be combined with a reference that teaches the use of a colloid. Specifically, the primary reference to Kipp teaches the use of a colloid which represents an incompatible teaching with Luddecke. Regardless whether it be process category one, two or three or subcategory Method A or B, Kipp teaches that an organic compound is dissolved in a first solvent or mixture of solvents. Examples of that fist solvent include polyvinylpyrrolidone and polypropylene alginate (.col. 6, lines 12 and 28). Polyvinylpyrrolidone and alginates are examples of colloids as defined by the '743 patent which are to be avoided in accordance with the express purpose of Luddecke, i.e., to dispense with a protective colloid. Furthermore, in accordance with Method A, one or more surfactants is added to the second aqueous phase (col, 6, lines 40-44). And in accordance with Method B, one or more surfactants is also added to the first solution (col. 8, lines 5-10). Examples of such surfactants include polyvinyl alcohol (col 70 lines 7-8), polyvinylpyrrolidone (col. 7, line 8) and methylcellulose (col, 7: line 5). Each of these surfactants is expressly defined by

the '743 patent as a colloid to be avoided in accordance with the express purpose of Luddecke, i.e., to dispense with a protective colloid. Further, Luddecke does not disclose or suggest the claimed process step of rapidly mixing a first solution comprising a substantially water-insoluble substance m a water-miscible organic solvent with an aqueous phase. Rather, Luddecke discloses mixing a carotenoid or retinoid with a water-miscible solvent within less than 10 seconds to form a first solution But there is no disclosure or suggestion of rapidly mixing that first solution with an aqueous phase as claimed. Example 1 of Luddecke discloses that the first solution after rapid mixing (0.35 sec) is metered at a rate of about 30 l/h into a second chamber and mixed with water. Again there is no disclosure or suggestion of rapid mixing with an aqueous phase as claimed.

However, in response to applicant's arguments with respect to the teachings in the '743 patent, it is of note that the '743 patent upon which applicant relies is not part of the invention of Luddecke. Luddecke is cited solely for the teachings of the rapid mixing technique. Further, in response to applicant's argument that *there is no disclosure or suggestion of rapid mixing with an aqueous phase as claimed*, it is noted that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Luddecke is not cited for the teachings of the aqueous phase, the composition recited in the claims is taught in Kipp.

Applicant argues that in contrast to the claimed invention, Lindrud does not disclose a step for forming a dispersion of amorphous particles. Rather, Lindrud is directed to *a continuous crystallization process* (p. 2, lines 24-28) which involves the formation of a crystallization slurry (p 5, lines 9-11). Lindrud applies ultrasound energy to the continuous crystallization process to form crystals having a diameter of less than one micron (Abstract, Examples 1 and 2). The Examiner appears to agree since the previous rejections under 35 US C §§ 102 and 103 in view Lindrud were withdrawn. The Examiner's reliance on any disclosure of rapid mixing by Luddecke is misplaced since the combination with Luddecke fails to alter the fact that Lindrud is directed to a continuous crystallization process. Again, the Examiner appears to agree since at page 5 of the Office Action, the Examiner states that Example I of Lindrud shows a temperature of 2°C *"throughout the crystallization".* Lindrud is silent whether or not an amorphous or crystalline suspension is formed. However, this is irrelevant since Lindrud cannot be modified without destroying its intended purpose and function, i.e., a continuous crystallization process.

However, in response to applicant's argument that *Lindrud does not disclose a step for forming a dispersion of amorphous particles*, it is noted that Lindrud teaches combining a solution of a pharmaceutical compound to be crystallized and an aqueous phase to form a precipitation (page 4, 2nd paragraph). The burden is shifted to applicant

to show that the precipitation taught by Lindrud process does not form amorphous particles. Applicant's attention is called to the teachings in the examples of Lindrud, where Lindrud teaches that the solution and the aqueous phase are mixed at maximum power level. This teaching of mixing at maximum power level reads over the claimed step of rapid mixing.

Applicant argues that Luddecke does not disclose or suggest the claimed process step of rapidly mixing a first solution comprising a substantially water-insoluble sub stance in a water-miscible organic solvent with an aqueous phase. Rather, Luddecke discloses mixing a carotenoid or retinoid with a water-miscible solvent within less than 10 seconds to form a first solution. But there is no disclosure or suggestion of rapidly mixing that first solution with an aqueous phase as claimed.

However, Luddecke is cited solely for the teachings of the rapid mixing technique. Further, in response to applicant's argument that *there is no disclosure or suggestion of rapid mixing with an aqueous phase as claimed*, it is noted that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to S. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 8:30 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. Tran/
Primary Examiner, Art Unit 1615